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Please find below and/or attached an Office communication concerning this application or proceeding.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/821,278
Filing Date: April 08, 2004
Appellant(s): LEONARD, THOMAS W.

Michael Sajovec
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed December 15, 2009 appealing from the Office action mailed March 2, 2009.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

An appeal brief has been filed for copending application 10/356,242.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

WITHDRAWN REJECTIONS

Upon the filing and acceptance of the terminal disclaimer, the double patenting rejection is herewith withdrawn. The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner. :

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 10-16 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 7427609 B2 to Leonard et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims encompass overlapping inventions, in that a method of treating vasomotor symptoms comprises administering a therapeutic amount of an estrogenic compound, and a therapeutic amount of progestational compound.

Claim 1 is also provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1and 6 of copending Application No.10/356,242. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims encompass overlapping inventions, in that a method of treating vasomotor symptoms comprises administering a

therapeutic amount of an estrogenic compound, and a therapeutic amount of progestational compound.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

20010034340	Pickar	10-2001
5798347	Labrie	08-1998
4381298	Coulson	4-1983

Prestwood et al. (The Effect of Low Dose Micronized 17 beta-Estradiol on Bone Turnover, Sex Hormone Levels, and Side Effects in Older Women: A Randomized, Double Blind, Placebo-Controlled Study. Journal of Clinical Endocrinology and Metabolism Vol. 85, NO.12)

Utian et al. (Efficacy and safety of low, standard, and high dosages of an estradiol transdermal system (Esclim) compared with placebo on vasomotor symptoms in highly symptomatic menopausal patients, American Journal Of Obstet Gynecol 1999 Jul;181(1):71-9)

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10-16, 19-23 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pickar (2001/0034340) in view of Labrie (5798347), Coulson (4381298), Prestwood et al. (The Effect of Low Dose Micronized 17-β-Estradiol on Bone Turnover, Sex Hormone Levels, and Side Effects in Older Women: A Randomized, Double Blind, Placebo-Controlled Study, *Journal of Clinical Endocrinology and Metabolism*, Vol. 85, No.12) and Utian et al. (Efficacy and safety of low, standard, and high dosages of an estradiol transdermal system (Esclim) compared with placebo on vasomotor symptoms in highly symptomatic menopausal patients, *American Journal Of Obstet Gynecol* 1999 Jul;181(1):71-9).

Pickar teaches a composition comprising preferably conjugated estrogens such as PREMARIN (conjugated equine estrogens, USP) and CENESTIN (synthetic conjugated estrogens, A), and medroxyprogesterone acetate (androgen and progestin) as an estrogen replacement therapy. PREMARIN (conjugated estrogens tablets, USP)

for oral administration contains a mixture of estrogens obtained exclusively from natural sources, occurring as the sodium salts of water-soluble estrogen sulfates blended. A mixture of sodium estrone sulfate and sodium equilin sulfate, and at least the following 8 concomitant components, also as sodium sulfate conjugates: 17- α-dihydroequilin, 17- α-estradiol,.δ-8,9-dehydroestrone, 17-β-dihydroequilin, 17-β- estradiol, equilenin, 17-α-dihydroequilenin, and 17-β-dihydroequilenin. PREMARIN is indicated in the treatment of moderate to severe vasomotor symptoms associated with the menopause. It is preferred that the dosage of PREMARIN is about 0.625 mg per day or less, and is more preferred that the dosage of PREMARIN is either about 0.45 mg per day or about 0.30 mg per day [0016] and a daily dose of medroxyprogesterone acetate in the amount of about 1.5 mg. The components of the combination are preferably administered at the same time; either as a unitary dosage form containing both components, or as separate dosage units; the components of the combination can be administered at different times during the day, provided that the desired daily dosage is achieved ([0011]).

The term "continuous and uninterrupted" means that there is no break in the treatment regimen, during the treatment period. Thus, "continuous, uninterrupted administration" of a combination, means that the combination is administered at least once daily during the entire treatment period. It is expected that the treatment period for the combination of conjugated estrogens and MPA will be for at least 30 days, preferably 120 days, and most preferably as long term treatment, and possibly indefinite, as one of the primary reasons for administering combinations of conjugated estrogens and MPA is to treat or inhibit menopausal or postmenopausal disorders.

Treatment periods also may vary depending on the symptoms to be treated. For example, for the treatment of vasomotor symptoms, it is preferred that the treatment may last from one month to several years, depending on the severity and duration of the symptoms [0020]. One aspect of this invention also covers situations in which a fixed daily dosage of the conjugated estrogens plus MPA combination is not given every day during the treatment period. For example, the dosage of a patient may need to be adjusted (either up or down), to achieve the desired effect during the middle of a treatment period [0022].

As these estrogens decline during the time preceding (perimenopause) and following the menopause (postmenopause), various physiological changes may result, including vulvar and vaginal atrophy causing vaginal dryness, pruritus and dyspareunia, and vasomotor instability manifested as hot flushes. Other menopausal disturbances may include depression, insomnia, and nervousness. Estrogen replacement therapy (ERT) is beneficial for symptomatic relief of hot flushes and genital atrophy and for prevention of postmenopausal osteoporosis.

Labrie is solely incorporated to show that medroxyprogesterone acetate is a progestin.

Coulson is solely incorporated to show that medroxyprogesterone acetate is an androgen.

Pickar fails to specifically teach the second dose of an estrogenic compound is administered after therapy of the vasomotor symptoms has been effectively established, wherein "the second dose of an estrogenic compound is administered between 2 weeks

and 12 weeks after the first dose of an estrogenic compound," "the second dose of an estrogenic compound is administered between 4 weeks and 8 weeks after the first dose of an estrogenic compound," "the first predetermined time period for said first dose of an estrogenic compound is at least twelve weeks before the administration of said second dose of an estrogenic compound," or "the first predetermined time period for said first dose of an estrogenic compound is at least four to eight weeks before the administration of said second dose of an estrogenic compound."

Prestwood et al. teaches the measure of serum and urinary biochemical markers of bone resorption and formation at baseline 6 and 12 weeks on treatment. Also, Prestwood et al. measured serum estradiol, estrone, and sex hormone-binding globulin levels at baseline, 12 weeks on treatment, and 12 weeks posttreatment. It was found that breast tenderness, bleeding, and endometrial changes were significantly less frequent in the 0.25 mg/day and placebo groups compared with the higher dose groups.

Additionally, Utian et al. teaches the main reason for changing to a lower dosage in ERT is to reduce estrogen side effects, especially genital bleeding and breast pain. It is therefore necessary to obtain a balance between relief of symptoms and the risk of adverse effects.

It would have been obvious to a skilled artisan to treat vasomotor symptoms comprising a first dose of a therapeutic amount of an estrogenic compound to a subject; and administering a second dose of a therapeutic amount of an estrogenic compound at a later time period to the subject, said second dose comprising a lower dosage of said therapeutic amount of an estrogenic compound than said first dose to produce the

required effect, i.e., to treat vasomotor symptoms. The motivation to administer the dosage in a first and lower second dosage or even a lower third dosage is because (1) Prestwood et al. teaches it was found that breast tenderness, bleeding, and endometrial changes were significantly less frequent in the 0.25 mg/day and placebo groups compared with the higher dose groups (2) Utian et al. teaches the main reason for changing to a lower dosage in ERT is to reduce estrogen side effects, especially genital bleeding and breast pain. It is therefore necessary to obtain a balance between relief of symptoms and the risk of adverse effects and (3) Pickar teaches the dosage of a patient may need to be adjusted (either up or down), to achieve the desired effect during the middle of a treatment period. Hence a skilled artisan would have had reasonable expectation of successfully producing the desired effect by adjusting the dosage.

(10) Response to Argument

A prima facie case of obviousness has been established. Appellant argues that the prima facie case of obviousness has not been established. In response to Appellants argument that the cited reference fails to disclose or suggest all of the recitations of the instant claims, and that it would not have been obvious to make and use, with expectation of success, that which is claimed based on the disclosures of the cited prior art, the Court has held that "the test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See *In re Rosselet*, 146 USPQ 183, 186 (CCPA 1965). "There is no

requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." *Motorola, Inc. v. Interdigital Tech. Corp.*, 43 USPQ2d 1481, 1489 (Fed. Cir. 1997). An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See *KSR Int'l Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Moreover, Appellant argues the Pickar et al. reference does not teach a (1) lower second dose and (2) the amounts of the first dose of the claimed invention. The Examiner's contention is that the rejection of record is not of anticipatory type but of obviousness type. (1) Hence, the teaching of Pickar et al. to adjust (either up or down) of the dose range to achieve the desired effect during the middle of a treatment period [0022] and further of Utian et al. to a lower dosage in ERT is to reduce estrogen side effects, especially genital bleeding and breast pain renders the claims obvious. (2)The Examiner states Pickar et al. clearly teaches about 0.625 mg per day or less and preferably about 0.45 mg per day to about 0.3 mg per day [0016] of the Premarin. Further, the claimed invention herein recites a first dose of 0.625 to 1.5 mg/day and a second dose of 0.05 to 0.625 mg (see claim 29). Hence, the amounts are not less than the prior art but in fact overlap.

The Appellant argues that the disclosure of Utian et al. "describe the disadvantages of starting estrogen replacement therapy (ERT) treatments with a high dose of estrogenic compounds. The preferred amounts as indicated by Pickar et al. and the disclosures of Utian et al. suggest that treatment be initiated a low doses. As such, the disclosures of Pickar et al. and Utian et al. teach away from a high first dose of an estrogenic compound in the ranges envisioned in the methods of the present invention." The Examiner respectfully reiterates the amounts claimed are not less than Pickar et al. but in fact overlap. Further, as taught by the primary reference Pickar et al., the dosage amount of an estrogenic compound in a patient may need to be adjusted (either up or down), to achieve the desired effect during the middle of a treatment period. [0022]. Hence, it is Examiners contention that although Utian et al. et al. states a "logical approach is to initiate treatment with a low dose of estradiol," the Appellant must consider the reference as a whole. The Utian et al. reference also states that the "use of a low-dosage patch may thus improve compliance without a significant loss of therapeutic benefit (page 78 col 2 lines 20-22)." Therefore, the Utian et al. reference in fact acknowledges that the sole use of a low-dosage regimen may improve compliance and that is with some loss of therapeutic benefit.

Appellant argues Pickar (2001/0034340), Labrie (5798347), Coulson (4381298), Prestwood et al., and Utian et al., and Hughes Jr. et al. do not describe all the limitations of the instant claims. However, Appellant has provided no evidence of record that all the limitations of the instant claims were not addressed.

The objective evidences on the record are not sufficient to overcome the obviousness rejections.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627

Conferees:

/Shengjun Wang/

Primary Examiner, Art Unit 1627

/S. J./

Examiner, Art Unit 1627